sulfonamide group, a lower alkylthio group or an optionally substituted amino group, or two of R_1, R_2, and R_3, together form an alkylenedioxide group;

R_4 represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

n is an integer of from 1 to 15;

or salts or solvates thereof.

REMARKS

Claims 9-13 and 14-17 have been amended to cancel subject matter corresponding to material of non-elected groups. Applicants reserve the right to pursue the cancelled subject matter in one or more divisional applications. No new matter has been introduced by virtue of these amendments.

Claims 13 and 15-18 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Applicants believe that the claims as amended are fully compliant with the requirements of 35 U.S.C. §112 including the requirements of 35 U.S.C. §112, second paragraph.

Reconsideration and withdrawal of each of the §112 rejections are thus requested.

Claims 9-14 were rejected under 35 U.S.C. §103(a) as being unpatentable over Hirai et al. [JP 04139172].

The rejection is traversed.

As the Office Action is understood, the position is taken that the cited documents report benzoxazole compounds which are allegedly related to Applicants' claimed subject matter. Moreover, the Examiner appears to take the position that the subject matter of claims 9-14 would have been obvious from the disclosure of structural isomers taught by Hirai.

Further, the Examiner asserts that the difference between the compounds of Hirai and the compounds of the present application are allegedly not non-obvious, i.e., that compounds having an "ethylene" group ($-CH_2CH_2-$) are obvious in view of the compounds recited by Hirai which have a "ethylidenyl" group ($-CH(CH_3)-$).

Applicants respectfully disagree. The compounds of the present invention comprise a two carbon linker (i) in which groups A (benzoxazole-Y-) and B (-amide-pyridyl group) are separated by two carbon atoms, e.g., A-CH_2CH_2-B. In contrast Hirai recites compounds in which groups A and B are separated by a linker (ii) having only one carbon atom between A and B, e.g., A-$CH(CH_3)$-B. Compounds having linking groups (i) and (ii) possess different spatial separtion between groups A and B such that the biological activity for compounds having linking group (i) cannot be predicted from compounds having linking group (ii).

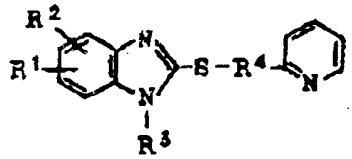
Isomers are different from each other in chemical and physical properties, and the properties of each compound would not be expected from the other. For example, it is well known that structural isomers possess different bond connectivities and consequently have different physical properties (including, for example, different melting points, polarities, conformations and the like) or different biological activities. Furthermore, stereoisomers, which possess the same structural connectivity, frequently possess vastly different physiological properties (See, for example, L-Dopa (drug for Parkinson's Disease) v. D-Dopa (no activity).

The compounds provided by the claims as amended possess ACAT inhibitor activity. In contrast, compounds recited by Hirai are alleged to possess anti-ulcer activity. More

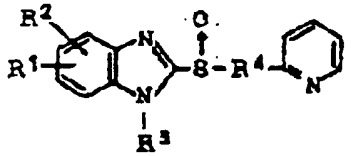
particularly, Hirai recites that the compounds disclosed therein have H^+ or K^+-ATPase inhibition activity. Clearly, the physiological activity of the claimed compounds and the compounds of Hirai are completely different.

Hirai teaches that the compounds disclosed therein offer improved anti-ulcer activity compared to the compounds recited in JP 54-141783-A. See, page 4 of the English language translation of Hirai. U.S. Patents 4,508,905, USP 4,337,257 and USP 4,255,431 are based on a U.S. application corresponding to JP 54-141783-A. A copy of pages 1 and 2 of U.S. Patent 4,255,431 (the '431 patent) are attached for the Examiner's consideration.

In the 431 patent, the following compounds are described as previously known compounds, represented by the formulas (I) and (II),



(I)



(II)

wherein R_4 represents a straight or branched C_{1-4} alkylene group having at least one methyl substituent.

JP 54-141783-A recites that the compounds having a substituted methylene group between the sulfoxide group and the pyridyl group, e.g., R_4 is a $-CH(R^6)-$ group, have superior physiological activity when compared to the physiological activity of compounds in which R_4 is

a methyl substituted C_{2-4}alkylene group. Moreover, JP 54-141783-A teaches that the antiulcer H^+,K^+-ATPase inhibition activity for compounds having a physiological activity of the compounds comprising a methyl substituted C_{2-4}alkylene group is different from the antiulcer H^+,K^+-ATPase inhibition activity for compounds in which R_4 is a -CH(R^6)- group, e.g., R_4 is a C_1 alkylidenyl group.

Applicants respectfully point out that this family of compounds includes structural isomers which have differences equivalent to the differences between the compounds of the instant invention and the compounds recited in Hirai. Thus, in view of JP 54-141783-A, the compounds of the instant invention would not have been obvious to one of ordinary skill in the art at the time the invention was made.

Accordingly, reconsideration and withdrawal of the §103 rejection are thus requested.

It is believed that the application is in condition for immediate allowance, which action is earnestly solicited.

Respectfully submitted,

January 21, 2003

John B. Alexander (Reg. No.: 48,399)
Dike, Bronstein, Roberts & Cushman IP Group
EDWARDS & ANGELL, LLP
P.O. Box 9169
Boston, MA 02209
Tel. (617) 439-4444

VERSION MARKED TO SHOW CHANGES

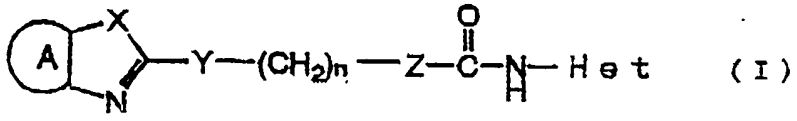
(Additions are underlined; deletions are bracketed.)

IN THE CLAIMS

Please cancel claim 13, without prejudice or disclaimer.

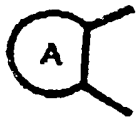
Claims 9-12 and 14-17 have been amended as follows:

9. (twice amended) Compounds represented by the formula (I)

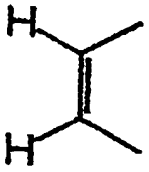


(I)

wherein



represents an optionally substituted divalent residue of benzene, [pyridine,]cyclohexane or naphthalene, or a group:



;

Het represents a substituted pyridyl group;

X represents [-NH-,]an oxygen atom[or a sulfur atom];

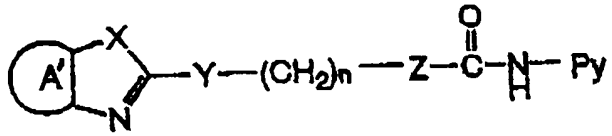
Y represents $-NR_4$ -, an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

Z represents a single bond;

R_4 represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

n is an integer of from 2 to 15, or salts or solvates thereof.

10. (twice amended) The compounds according to claim 9, which are represented by the formula (IA)



(I A)

wherein

represents an optionally substituted divalent residue of [benzene or pyridine];

Py represents a substituted pyridyl group;

X represents [-NH-,]an oxygen atom[or a sulfur atom];

Y represents -NR_4-, an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

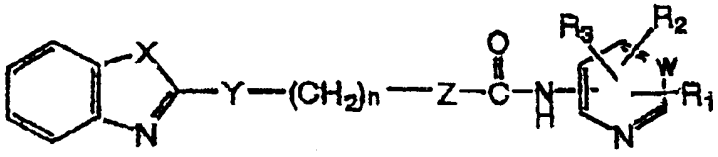
Z represents a single bond;

R_4 represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

n is an integer of from 2 to 15;

or salts or solvates thereof.

11. (twice amended) The compounds according to claim 9, which are represented by the formula (III)



(III)

wherein, W represents =CH-;

X represents [-NH-,]an oxygen atom[or a sulfur atom];

Y represents $-NR_4-$, an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

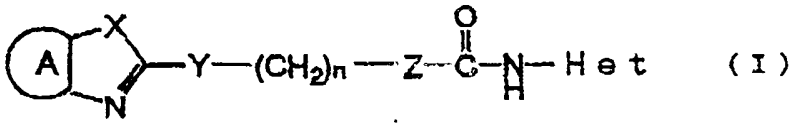
Z represents a single bond;

R_1, R_2, and R_3 are the same or different, and each represents a hydrogen atom, a lower alkyl group, a lower alkoxy group, a halogen atom, a hydroxyl group, a phosphate group, a sulfonamide group, a lower alkylthio group or an optionally substituted amino group, or two of R_1, R_2, and R_3, together form an alkylenedioxide group, provided that R_1, R_2 and R_3 are not hydrogen at the same time;

R_4 represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

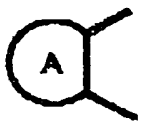
n is an integer of from 2 to 15, or salts or solvates thereof.

12. (twice amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and at least one compound selected from the compounds represented by the formula (I)

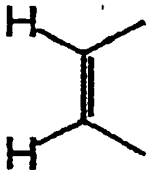


(I)

wherein



represents an optionally substituted divalent residue of benzene, [pyridine,]cyclohexane or naphthalene, or a group:



;

Het represents a substituted pyridyl group;

X represents [-NH-,]an oxygen atom[or a sulfur atom];

Y represents -NR-, an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

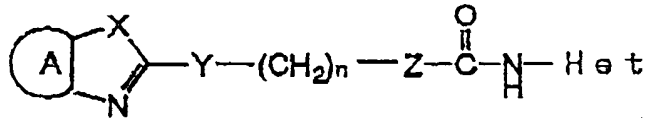
Z represents a single bond;

R_4 represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

n is an integer of from 2 to 15, or salts or solvates thereof.

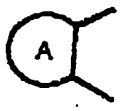
14. (amended) The pharmaceutical composition according to claim 12 or 13, which is a remedy or a medication for preventing hyperlipemia, arteriosclerosis, cerebrovascular accidents, ischemic heart disease, ischemic intestinal disease or aortic aneurysm.

15. (twice amended) [The]A method for treating hyperlipemia, arteriosclerosis, cerebrovascular accidents, ischemic heart disease, ischemic intestinal disease or aortic aneurysm [in need of such treatment] by administering to a patient in need of such treatment a compound of the formula (I')

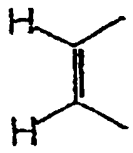


(I')

wherein



represents an optionally substituted divalent residue of benzene, [pyridine,]cyclohexane or naphthalene, or a group:



;

Het represents substituted or unsubstituted pyridyl [or pyrimidyl]group;

X represents [-NH-,]an oxygen atom[or a sulfur atom];

Y represents -NR_4-, an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

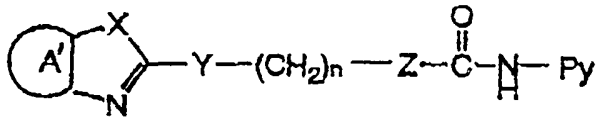
Z represents a single bond;

R_4 represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

n is an integer of from 1 to 15;

or salts or solvates thereof.

16. (twice amended) The method of claim 15 wherein a compound of formula (I'A) is administered



(I'A)

wherein

represents an optionally substituted divalent residue of benzene [or pyridine];

Py represents an optionally substituted pyridyl [or pyrimidyl]group;

X represents [-NH-,]an oxygen atom[or a sulfur atom];

Y represents -NR_4-, an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

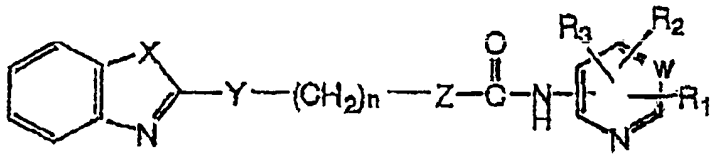
Z represents a single bond;

R_4 represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group;

n is an integer of from 1 to 15,

or salts or solvates thereof.

17. (twice amended) The method of claim 15 wherein a compound of formula (III') is administered



(III')

wherein, W represents =CH- [or =N-],

X represents [-NH-,]an oxygen atom[or a sulfur atom];

Y represents -NR_4- an oxygen atom, a sulfur atom, a sulfoxide or a sulfone;

Z represents a single bond;

R_1, R_2, and R_3 are the same or different, and each represents a hydrogen atom, a lower alkyl group, a lower alkoxy group, a halogen atom, a hydroxyl group, a phosphate group, a sulfonamide group, a lower alkylthio group or an optionally substituted amino group, or two of R_1, R_2, and R_3, together form an alkylenedioxide group;

R_4 represents a hydrogen atom, a lower alkyl group, an aryl group or an optionally substituted silyl lower alkyl group; and

n is an integer of from 1 to 15;

or salts or solvates thereof.